REMARKS

The Patent and Trademark Office withdrew the rejections of the claims made under 35 USC §103(a), §112, first paragraph, and §112, second paragraph in light of the amendments and remarks of the prior Office Action response. Applicants intend to address similarly all remaining rejections and objections to achieve a speedy allowance.

Amendments

Claims 1 and 46 have been amended to recite 15-25% transduction efficiency of GEM WT. This is supported in the specification at page 44, lines 4-5, which teaches: "There has been a report that the LV cavity injection method resulted in a transduction efficiency of 15-25% in the heart. See Miake, J. et al. J Clin Invest 111, 1529-36 (2003)." Claims 1 and 47 now recite the GEM mutant W269G.

Claim Objections

The Patent and Trademark Office objected to claims 1, 46, and 47 due to wording in the preamble. Applicant has amended the claims to address this, and consequently requests withdrawal of the objection.

Claim Rejections - 35 USC §112, first paragraph - Enablement

The Patent and Trademark Office rejected claims 1-4, 6, 20-34, 42, 46-48, and 77-82 under 35 USC §112, first paragraph for failing to comply with the enablement requirement.

The Patent and Trademark Office recognizes that applicant has taught that the full-length GEM WT sequence and the W269G mutant modulate calcium channel activity. "Applicants through their working examples, have only taught that full-length and the less-effective mutant W269G have exhibited any modulation of calcium channel activity." Office Action at page 4. However, the Patent and Trademark Office expresses concern that administration of the full-length GEM WT sequence is lethal to some animals.

Applicant respectfully disagrees with the Patent and Trademark Office's characterization of claims 1-4, 6, 20-34, 42, 46-48, and 77-82 as being non-enabling. However, to expedite prosecution, applicant has amended independent claims 1, 46, and 47 to recite, *inter alia*, a method for modulating calcium channel activity comprising:

- contacting the excitable cells with a nucleic acid encoding a GEM protein having an amino acid sequence according to SEQ ID NO.: 1, such that 15%-25% of the excitable cells are transduced (claims 1 and 46);

or

- a nucleic acid encoding a variant of the GEM protein comprising an amino acid substitution of glycine for tryptophan at position 269 of SEQ ID NO.: 1 (claims 1 and 47).

In contrast to the transduction efficiency of 60% discussed in Example 4, which was lethal to some animals, the 15-25% transduction efficiency is not lethal. As shown in the specification, animals transduced with WT GEM at this level of efficiency survive and demonstrate altered calcium channel activity (abbreviated QTc intervals measured on EKG). See Example 2. Murata *et al.*, *Circ. Res.* (2004) vol. 95, pg. 389-405, a paper published after the filing of the present application, similarly reports that the injection of adenovirus constructs carrying reporter genes achieves cardiac myocycte transduction efficiency of 15-25%. The administration of viruses carrying nucleic acids that encode the WT GEM protein, when transduced at levels of 15-25% result in modulated calcium channel activity, without the lethal effect sometimes observed with higher transduction levels.

Independent claims 1 and 47 recite the W269G variant of the SEQ ID NO.: 1 protein. This variant is non-lethal and results in modulated calcium channel activity. Example 4 shows that cardiac-specific expression of W269G attenuates myocyte and organ hypertrophy, ameliorates ventricular dysfunction, and suppresses fibrosis during pathological pressure overload.

In light of the amendments to independent claims 1, 47, and 48, the specification provides all necessary structural information and functional characteristics to enable the artisan to practice the methods as claimed without the need for undue experimentation. Applicant therefore respectfully requests withdrawal of the rejection.

Claim Rejections - 35 USC §112, first paragraph - Written Description

The Patent and Trademark Office also rejected claims 1-4, 6, 20-34, 42, 46-48, and 77-82 under 35 USC §112, first paragraph, for failing to comply with the written description requirement. The Patent and Trademark Office indicated that the specification failed to teach possession of any protein that is less than 100% identical with SEQ ID NO.: 1 that exhibits modulation of a calcium channel in a cell (Office Action, page 9).

Although applicant does not agree with the Patent and Trademark Office's characterization of the claims as failing to meet the written description requirement, applicant has amended independent claims 1, 46, and 47 to recite two forms of GEM protein. The specification clearly discloses the full polypeptide sequence of SEQ ID NO.: 1 and the W269G mutant, a defined variant of SEQ ID NO.:1 (see page 29, lines 25-29 and page 33, lines 3-6 of the specification). Thus, applicant had possession of the two amino acid sequences recited in the amended claims at the time the application was filed. Applicant respectfully requests that the rejection be withdrawn.

No Disclaimers or Disavowals

Although the present and previous communications may include or have included alterations to the application or claims, or characterizations of claim scope or referenced art, the applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant expressly reserves the right to pursue later any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed in this application or by any prior application. Accordingly, reviewers of this or any parent, child, or related prosecution history cannot reasonably infer that applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Other U.S. Patents and Applications

Applicant provides the following table to aid the Patent and Trademark Office during prosecution. The following U.S. patents and patent applications have at least one listed inventor or assignee in common with the above-captioned application or a patent/application identified on the table:

ATT'Y DOCKET NO.	**SERIAL NO.**	**FILE DATE**	**TITLE**
439	10/092,184	03/05/2002	Gene Delivery Compositions and Methods
441	09947953	09/06/2001	Cardiac Arrhythmia Treatment Methods
449	9977865	10/15/2001	Methods and Compositions for Nucleic Acid Delivery
454	10476259	10/27/2003	Biological Pacemaker
465	9169739	10/08/1998	Gene Delivery Compositions and Methods
471	10855989	05/28/2004	Cardiac Arrhythmia Treatment Methods
472	10855892	05/28/2004	Cardiac Arrhythmia Treatment Methods
473	10855805	05/28/2004	Cardiac Arrhythmia Treatment Methods
516	11/007,315	12/09/2004	Gene Delivery Compositions and Methods
610	11/508957	08/24/2006	Cardiac Arrhythmia Treatment Methods
671	11/905,757	10/03/2007	Focal Calcium Channel Modulation
690	12/035,077	02/21/2008	Cardiac Arrhythmia Treatment Methods and Biological Pacemaker
696	12/089,460	04/07/2008	Biologically Excitable Cells
83648	9407945	9/29/1999	Inducible Genetic Suppression of Cellular Excitability

Copies of these patents and patent applications, including any pending claims, office actions, allowances, and/or other communications, are available through PALM and/or PAIR. However, if the Patent and Trademark Office so requests, applicant will be happy to provide the Patent and Trademark Office with copies of any applications, pending claims, office actions, allowances, communications or any other documents, at any time.

The claims of the present application are different and may be broader in scope than the claims in any related patent or application. To the extent that any statements made in a related case (such as amendments or characterizations regarding the scope of a claim or prior art) could be construed as a disclaimer of any subject matter supported by the present disclosure, applicant rescinds and retracts such disclaimer. Accordingly, any listed or cited reference in a prior or related application may need to be reviewed with regard to the present claims. Further, any objections or rejections made by the Patent and Trademark Office in the issued and allowed cases identified above may need to be reviewed with regard to the present application.

Respectfully submitted,

Dated: September 4, 2009

By: ***/Sarah A. Kagan /***
Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No. 22907

Enclosure: Murata et al., Circ. Res. 95:398-405, 2004